09/743,954

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Thursday, August 19, 2004

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L8	L7 and (venom$ or apamin$ or tertiapin$ or degranulating)	2
☐	L7	L6 and lu	44
☐	L6	(trustees)near5(pennsylvania or pa)	837
☐	L5	(tertiapin$)	10
☐	L4	(tertiapin$)near3(derivativ$ or analog$ or modified or modify or mutate$ or mutant$)	1
☐	L3	(tertiapin$ or apamin$).ti.	13
☐	L2	l1 and (tertiapin$)near3(derivativ$ or analog$ or modified or modify or mutate$ or mutant$)	1
☐	L1	lu and (tertiapin$ or apamin? or bee or venom$)	11905

END OF SEARCH HISTORY

09/743,054

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     (FILE 'HOME' ENTERED AT 10:12:43 ON 19 AUG 2004)

     FILE 'REGISTRY' ENTERED AT 10:13:02 ON 19 AUG 2004
L1            2 S ALCNCNRIIIPHQCWKKCGKK/SQSP        seq 2

     FILE 'CAPLUS, TOXCENTER, USPATFULL' ENTERED AT 10:14:20 ON 19 AUG 2004
L2            6 S L1
L3            4 DUP REM L2 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 10:17:41 ON 19 AUG 2004

     FILE 'REGISTRY' ENTERED AT 10:20:24 ON 19 AUG 2004
L4            4 S ALCNCNRIIIPHMCWKKCGKK/SQSP        seq 1

     FILE 'AGRICOLA, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, MEDLINE,
     TOXCENTER, USPATFULL' ENTERED AT 10:22:16 ON 19 AUG 2004
L5          133 S L4
L6            0 S L5 AND PHARMACEUTICAL?
L7            5 S L5 AND TREAT?
L8            3 DUP REM L7 (2 DUPLICATES REMOVED)
L9           13 S L5 AND (DERIVATIVE? OR ANALOG? OR MODIFY OR MODIFIED OR MUTA
L10           5 DUP REM L9 (8 DUPLICATES REMOVED)

     FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 10:26:10 ON 19
     AUG 2004
L11           1 S TERTIAPIN? AND PHARMACEUTICAL?
L12          59 S APAMIN? AND PHARMACEUTICAL?
L13           3 S (APAMIN?)(23A)(PHARMACEUTICAL?)
L14           4 S (APAMIN?)(50A)(PHARMACEUTICAL?)
L15           1 S L14 NOT L13
L16          55 S (TERTIAPIN?) AND PHARM?
L17          35 DUP REM L16 (20 DUPLICATES REMOVED)
L18          10 S L17 AND (TERTIAPIN?)/TI
L19        1405 S (APAMIN?)/TI
L20         495 S L19 AND PHARM?
L21           7 S L19 AND PHARMACEUT?
L22           7 DUP REM L21 (0 DUPLICATES REMOVED)
L23           4 S G1RK?
L24         564 S ROMK1?
L25         184 S L24 AND INHIBIT?
L26           0 S L25 AND PHARMACEUT?
L27          11 S L25 AND PEPTID?
L28           8 DUP REM L27 (3 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 10:38:04 ON 19 AUG 2004

     FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 10:42:19 ON 19
     AUG 2004
L29        1367 S (APAMIN)/TI
L30          97 S L29 AND (BEE)/TI
L31          93 S L30 AND (VENOM)/TI
L32          26 S L31 AND (PEPTIDE?)/TI
L33           9 DUP REM L32 (17 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 10:47:25 ON 19 AUG 2004

     FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 10:49:05 ON 19
     AUG 2004
L34        2838 S (MELITTIN)/TI
L35           6 S L34 AND PHARMACEUTICAL?
L36           6 DUP REM L35 (0 DUPLICATES REMOVED)
L37       10113 S (LU, Z? OR LU Z?)/AU,IN
L38          46 S L37 AND VENOM?
```

L39 24 DUP REM L38 (22 DUPLICATES REMOVED)

=>

(32) Mackinnon, R; J Gen Physiol 1988, V91, P335 CAPLUS
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=>

(composition; tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT Potassium channel
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(inward-rectifier, GIRK1/4 and **ROMK1**; tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT Honeybee
Venoms
(purification of tertiapin from honeybee venom; tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT Molecular association
(tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT 24345-16-2, Apamin 83856-13-7, Mast cell degranulating **peptide**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(comparison; tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT 63-68-3, L-Methionine, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(functional role of residue Met13; tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

IT 58694-52-3P, Tertiapin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(tertiapin is a novel high-affinity **inhibitor** for inward-rectifier K+ channels)

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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ORGN Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Escherichia-coli
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Salientia 85306
Super Taxa
Amphibia; Vertebrata; Chordata; Animalia
Organism Name
Xenopus-laevis
Taxa Notes
Amphibians, Animals, Chordates, Nonhuman Vertebrates, Vertebrates
ORGN Classifier
Serpentes 85410
Super Taxa
Reptilia; Vertebrata; Chordata; Animalia
Organism Name
Dendroaspis-angusticeps
Taxa Notes
Animals, Chordates, Nonhuman Vertebrates, Reptiles, Vertebrates
RN 7440-09-7 (POTASSIUM)
8016-13-5 (PROMEGA)
83453-41-2 (MONOS)

=> d 5 all

L28 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:556295 CAPLUS
DN 129:272022
ED Entered STN: 02 Sep 1998
TI A Novel High-Affinity **Inhibitor** for Inward-Rectifier K+ Channels
AU Jin, Weili; Lu, Zhe
CS Department of Physiology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Biochemistry (1998), 37(38), 13291-13299
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
CC 6-3 (General Biochemistry)
AB Inward-rectifier K+ channels are a group of highly specialized K+ channels that accomplish a variety of important biol. tasks. Inward-rectifier K+ channels differ from voltage-activated K+ channels not only functionally but also structurally. Each of the four subunits of the inward-rectifier K+ channels has only two instead of six transmembrane segments compared to the voltage-activated K+ channels. Thus far, there are no high-affinity ligands that directly target any inward-rectifier K+ channel. In the present study, we identified, purified, and synthesized a protein **inhibitor** of the inward-rectifier K+ channels. The **inhibitor**, called tertiapin, blocks a G-protein-gated channel (GIRK1/4) and the **ROMK1** channel with nanomolar affinities, but a closely related channel, IRK1, is insensitive to tertiapin. Mutagenesis studies show that tertiapin **inhibits** the channel by binding to the external end of the ion conduction pore.
ST tertiapin **inhibitor** inward rectifier potassium channel
IT Amino acids, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

L28 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:518914 BIOSIS
DN PREV199800518914
TI A snake toxin **inhibitor** of inward rectifier potassium channel **ROMK1**.
AU Imredy, John P.; Chen, Chinfei; Mackinnon, Roderick [Reprint author]
CS Box 47, 1230 York Ave., New York, NY 10021, USA
SO Biochemistry, (Oct. 20, 1998) Vol. 37, No. 42, pp. 14867-14874. print.
CODEN: BICHAW. ISSN: 0006-2960.
DT Article
LA English
ED Entered STN: 18 Dec 1998
Last Updated on STN: 10 May 1999
AB Mamba snake dendrotoxins have been used extensively in biochemical and physiological studies of K+ channels of the brain. Their known targets of **inhibition** have been limited to the family of voltagegated K+ channels. We report the isolation of a dendrotoxin **inhibitor** of **ROMK1**, a channel belonging to the inward rectifier family of K+ channels. The **inhibitory** activity, fractionated to purity with FPLC and HPLC, is identical to a previously identified 6-dendrotoxin. To verify that 6-dendrotoxin blocks **ROMK1** channels, a cDNA encoding the toxin was synthesized and recombinant toxin expressed in Escherichia coli. Electrophysiological recordings reveal that recombinant 6-dendrotoxin has a half-maximal **inhibition** constant (Kd) of 150 nM when applied to **ROMK1** channels expressed in Xenopus laevis oocytes. That the 6-dendrotoxin binding site exists on separate K+ channel classes is shown by its high affinity for two of the voltage-gated family of channels, Kv1.1 (Kd < 0.1 nM) and Kv1.6 (Kd = 23 nM). Single amino acid substitutions in **ROMK1** indicate that 6-dendrotoxin binds to the pore region of **ROMK1** even though it does not completely block conduction through the pore. These results suggest that dendrotoxins **inhibit** K+ channels by recognizing the structurally conserved pore region of these channels.
CC Toxicology - General and methods 22501
Cytology - Animal 02506
Biochemistry methods - General 10050
Biochemistry studies - General 10060
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Toxicology
IT Parts, Structures, & Systems of Organisms
oocytes: reproductive system
IT Chemicals & Biochemicals
cDNA [complementary DNA]: expression, synthesis; delta-dendrotoxin: expression, recombinant, toxin, purification; pBluescript plasmid: Stratagene, expression vector; pCDNA/Amp plasmid: Invitrogen, expression vector; pGEM plasmid: Promega, expression vector; Dendroaspis angusticeps venom: analysis, purification, toxin; Kv1.1: analysis, voltage-gated channel; **ROMK1**: analysis, **inhibition**, pore region, inward rectifier potassium channel
IT Methods & Equipment
amino acid analysis: Analysis/Characterization Techniques: CB, analytical method; electrophysiological recording: Analysis/Characterization Techniques: CT, analytical method; mass spectrometry: analytical method, spectroscopic techniques: CB; **peptide** sequencing: sequencing method, sequencing techniques; reversed-phase HPLC [reversed-phase high performance liquid chromatography]: high performance liquid chromatography, purification method; C18 reverse-phase column: high performance liquid chromatography, purification method; Edman degradation: protein sequencing, sequencing method; MonoS FPLC column: Pharmacia, laboratory equipment; SDS-PAGE [SDS-polyacrylamide gel electrophoresis]: analytical method, gel electrophoresis

L28 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:329351 CAPLUS
DN 126:339864
ED Entered STN: 24 May 1997
TI Purification, Characterization, and Synthesis of an Inward-Rectifier K+ Channel **Inhibitor** from Scorpion Venom
AU Lu, Zhe; MacKinnon, Roderick
CS Department of Neurobiology, Harvard Medical School, Boston, MA, 02115, USA
SO Biochemistry (1997), 36(23), 6936-6940
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
CC 4-5 (Toxicology)
AB We have purified a **peptide inhibitor** of an inward-rectifier K+ channel, **ROMK1**, from the venom of the scorpion Leiurus quinquestriatus var. hebraeus. The **inhibitor** is Lq2, a previously discovered blocker of voltage- and Ca2+-activated K+ channels. Mutations were made on the channel and the **inhibitor**, and the resulting effects were examined using an electrophysiol. assay. The data show that Lq2 blocks the pore of **ROMK1**, and that the interaction surface on Lq2 is the same for binding to inward-rectifier, voltage-activated, or Ca2+-activated K+ channels. These findings support the notion that different classes of K+ channels have different gates but a similar K+-selective pore structure.
ST potassium channel **inhibitor** scorpion venom toxin
IT Toxins
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(Lq2; purification, characterization, and synthesis of inward-rectifier K+ channel **inhibitor** from scorpion venom)
IT Potassium channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ROMK1**; purification, characterization, and synthesis of inward-rectifier K+ channel **inhibitor** from scorpion venom)
IT Leiurus quinquestriatus hebraeus
Venoms
(purification, characterization, and synthesis of inward-rectifier K+ channel **inhibitor** from scorpion venom)
IT Amino acids, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(purification, characterization, and synthesis of inward-rectifier K+ channel **inhibitor** from scorpion venom)

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09/743,054

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      (FILE 'HOME' ENTERED AT 08:34:57 ON 19 AUG 2004)

      FILE 'REGISTRY' ENTERED AT 08:35:11 ON 19 AUG 2004
                E (APAMIN)/CN
                E APAMIN/CN
L1              1 S E3
L2              6 S CNCNRIIIPH[MQ]CWKK/SQSP

      FILE 'AGRICOLA, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, MEDLINE,
      TOXCENTER, USPATFULL' ENTERED AT 08:39:50 ON 19 AUG 2004
L3            136 S L2

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L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   254427-94-6  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
           === === === === === === === === === ===
        11 Pro-His-Gln-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === === === ===
        21 Lys
           ===
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L1   ANSWER 2 OF 2  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   252258-78-9  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
           === === === === === === === === === ===
        11 Pro-His-Gln-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
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        21 Lys
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HITS AT:   1-21
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L2   ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   403843-29-8  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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        11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === ===
        21 Lys
HITS AT:   3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L2   ANSWER 2 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   254427-94-6  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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        11 Pro-His-Gln-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === ===
        21 Lys
HITS AT:   3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L2   ANSWER 3 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   252258-78-9  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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           === === === === === === === ===
        21 Lys
HITS AT:   3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L2   ANSWER 4 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   228579-60-0  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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        11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === ===
        21 Lys
HITS AT:   3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L2   ANSWER 5 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   228579-40-6  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
                   === === === === === === === ===
        11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === ===
        21 Lys
HITS AT:   3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L2   ANSWER 6 OF 6  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   58694-52-3  REGISTRY
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SEQ3      1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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         11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
            ===  ===  ===  ===  ===  ===  ===
         21 Lys
HITS AT:    3-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**


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L4   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   403843-29-8  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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           === === === === === === === === === ===
        21 Lys
           ===
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L4   ANSWER 2 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   228579-60-0  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
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           === === === === === === === === === ===
        21 Lys
           ===
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L4   ANSWER 3 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   228579-40-6  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
           === === === === === === === === === ===
        11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === === === ===
        21 Lys
           ===
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

L4   ANSWER 4 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   58694-52-3  REGISTRY

SEQ3     1 Ala-Leu-Cys-Asn-Cys-Asn-Arg-Ile-Ile-Ile-
           === === === === === === === === === ===
        11 Pro-His-Met-Cys-Trp-Lys-Lys-Cys-Gly-Lys-
           === === === === === === === === === ===
        21 Lys
           ===
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
```

L8 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 139:391382 CA
TI A method of **treating** or reducing cell death, especially neuronal cell death, by administering an ion channel blocking agent
IN Bartlett, Perry Francis; Coulson, Elizabeth Jane; Morley, Samuel Nicholas; Hulett, Sarah Marie
PA The Walter and Eliza Hall Institute of Medical Research, Australia
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003094903	A1	20031120	WO 2003-AU580	20030514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI AU 2002-2307 A 20020514
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 1999:636933 CAPLUS
DN 132:32346
TI Synthesis of a Stable Form of Tertiapin: A High-Affinity Inhibitor for Inward-Rectifier K+ Channels
AU Jin, Weili; Lu, Zhe
CS Department of Physiology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Biochemistry (1999), 38(43), 14286-14293
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 4 hit

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
IT **252258-78-9P**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis of a stable form of tertiapin, a high-affinity inhibitor for inward-rectifier K+ channels)

=> d 4 ab

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AB Tertiapin (TPN), a small protein derived from honey bee venom, inhibits the GIRK1/4 and ROMK1 channels with nanomolar affinities. Methionine residue 13 in TPN interacts with residue F148 in the channel, located just outside of the narrow region of the ROMK1 pore. The methionine residue in TPN can be oxidized by air, which significantly hinders TPN binding to the channels. To overcome the reduction in TPN affinity due to oxidation of M13, we replaced M13 in TPN with fourteen different residues. Out of the fourteen derivs., only the one in which M13 was replaced by glutamine, TPNQ, binds to the channel with a Ki value very similar to that of native TPN. Since TPNQ is stable and functionally resembles native TPN, it will be a very useful mol. probe for studying the inward-rectifier K+ channels.

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